

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
8 June 2006 (08.06.2006)

PCT

(10) International Publication Number
WO 2006/059781 A1

(51) International Patent Classification:
C07D 215/22 (2006.01)

(21) International Application Number:
PCT/JP2005/022412

(22) International Filing Date:
30 November 2005 (30.11.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
2004-348425 1 December 2004 (01.12.2004) JP

(71) Applicant (for all designated States except US): OTSUKA
PHARMACEUTICAL CO., LTD. [JP/JP]; 9, Kandat-
sukasa-cho 2-chome, Chiyoda-ku, Tokyo, 1018535 (JP).

(72) Inventors; and

(75) Inventors/Applicants (for US only): NISHITANI, Shinji
[JP/US]; c/o Otsuka Maryland Research Institute, Inc.,
2440 Research Boulevard, Rockville, Maryland, 20850
(US). FUKUDA, Norio [JP/JP]; c/o OTSUKA PHAR-
MACEUTICAL CO., LTD., 224-18, Hiraishi-Ebisuno,
Kawauchi-cho, Tokushima-shi, Tokushima, 7710132 (JP).

(74) Agents: KAWAMIYA, Osamu et al.; AOYAMA &
PARTNERS, IMP Building, 3-7, Shiromi 1-chome,
Chuo-ku, Osaka-shi, Osaka 5400001 (JP).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV,
LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG,
SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US,
UZ, VC, VN, YU, ZA, ZM, ZW.

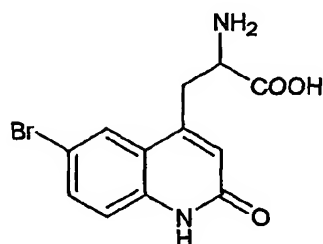
(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,
FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT,
RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA,
GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

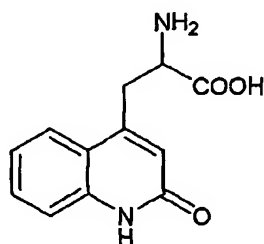
— with international search report

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

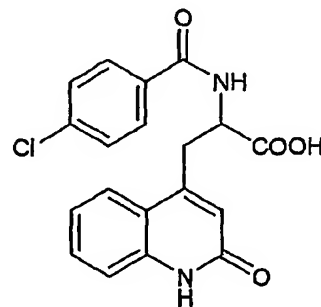
(54) Title: IMPROVED PROCESS FOR PREPARING REBAMIPIDE



(11)



(5)



(1)

(57) Abstract: The invention provides an improved process for preparing rebamipide that is useful as a medicament, which makes it possible to prepare rebamipide with high purity and high yield. The invention is an improved process for preparing rebamipide of the formula (1), comprising subjecting a carbostyryl amino acid compound of the formula (5) or a salt thereof containing a compound of the formula (11) as an impurity to a reduction treatment in the presence of hydrogen and a catalyst in a basic aqueous solution, thereby selectively reducing the impurity compound (11) to transform into the carbostyryl amino acid compound (5); and then acylating the compound (5) in a basic aqueous solution to give rebamipide (1).